"Synopsis of proposed Ph.D. research work"

Development of Novel Methods for Diversely Functionalized Heterocycles

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Development of Novel Methods for Diversely Functionalized Heterocycles

Origin of the research problem:

Polysubstituted furan derivatives are an important class of heterocycles and widely distributed in nature.[1] These are served as useful building blocks for various biologically active molecules, functional materials, agrochemicals as well as useful intermediates in organic synthesis (Fig. 1).[2]

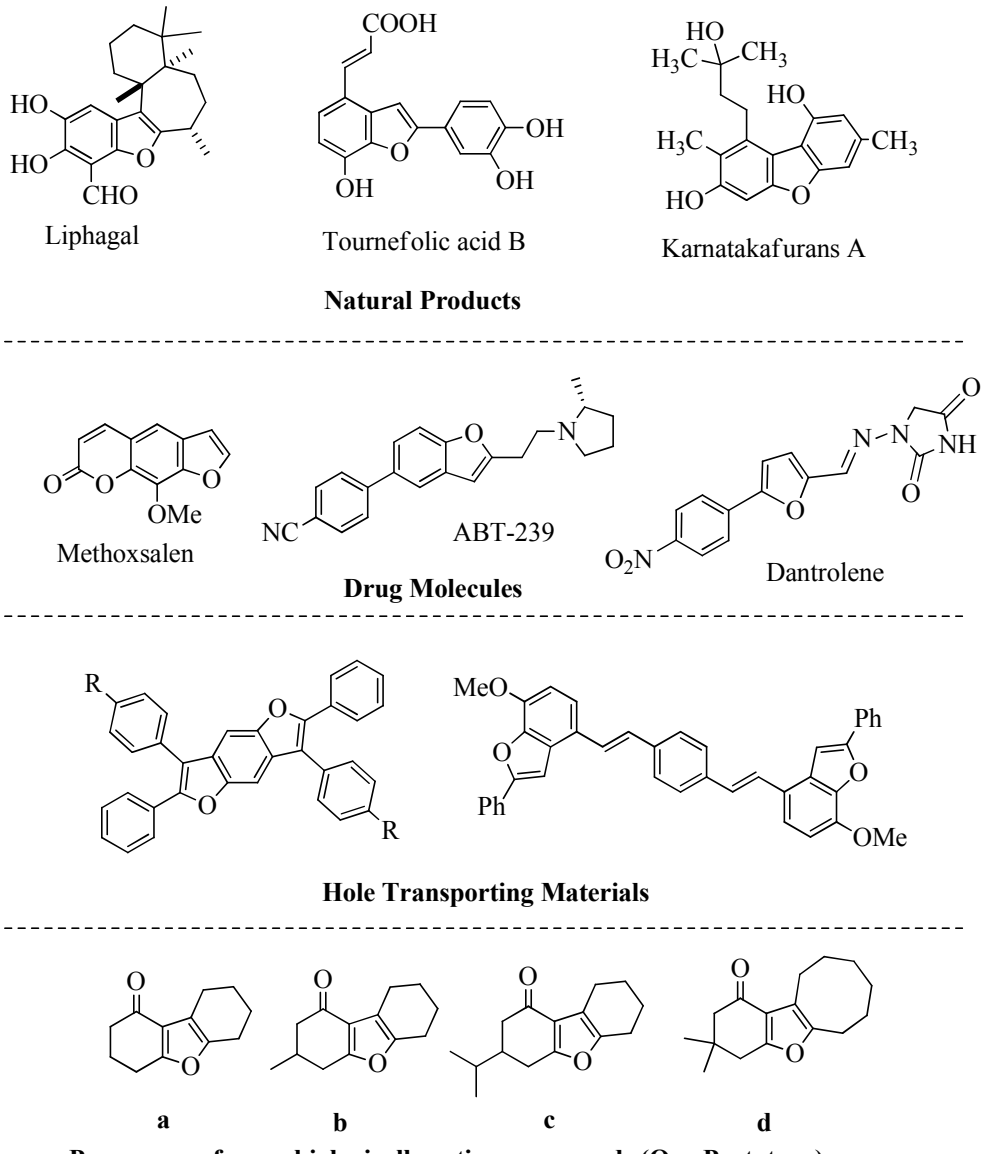
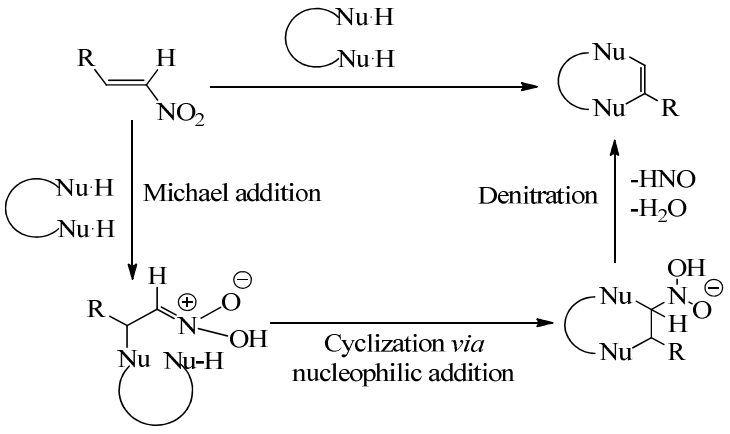


Fig. 1 Furan containing important molecules.

Several methodologies have been developed to synthesize furan derivatives considering their wide range of activities. The important classical approaches are Paal-Knorr synthesis and Feist-Benary synthesis[4] which have been established for the assembly of polysubstituted furans from dicarbonyl compounds. Prefunctionalized acyclic ketone derivatives like α-aryloxyketones, *o*-alkoxyketones, cyclopropenyl ketones, allenyl ketones, β-acyloxy acetylenic ketones[5] *etc*. are also been employed as the key starting materials for the construction of this scaffold. However, these functionalized precursors are generally synthesized through specialized protocols involving multi-step procedures. Transition metal-catalyzed synthetic strategies involving inter/intramolecular couplings are also very effective for the synthesis of furan derivatives.[6] Arenofurans are another important class of heterocycles and many strategies have been developed towards the synthesis of these derivatives. Most of the reported methods involved transition metal as catalyst and phenols or its derivatives as the starting materials.[7] However, practical and general methods for the synthesis of these derivatives are limited. Therefore, developing a new strategy for the synthesis of furan derivatives in terms of using basic chemicals as starting materials, increasing efficiency and generality, operational simplicity, and economic practicability is highly desirable.

Conjugated nitroalkenes are efficient Michael acceptors due to high electrophilicity of the double bond. These are also used as versatile substrates in various organic transformations. In addition, nitroalkenes are capable of binucleophilic addition to form various heterocycles and carbocycles in a cascade fashion *via* Michael addition/cyclization/denitration (Scheme 1).



Scheme 1: Mode of activity of nitrostyrenes.

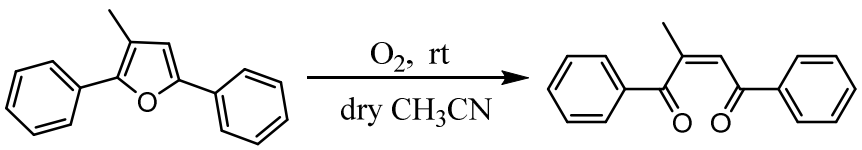
In this context, Chen *et al*. and Namboothiri *et al*. independently explored the reactive nitroallylic acetate (Morita-Baylis-Hillman acetates of nitroalkenes) for the synthesis of furan derivative.

Objective(s) of the work:

We wish to develop an efficient and general method for the synthesis of mainly substituted furans and indoles under environmentally benign conditions.

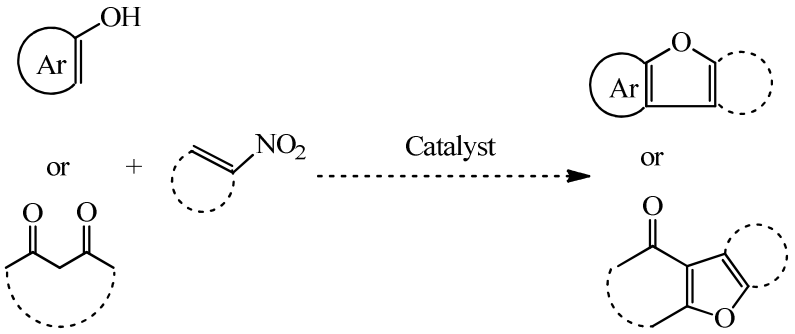
Methodology:

Dicarbonyl derivatives are important building blocks for the construction of biologically active compounds.[8] But-2-ene-1,4-dione which are important Intermediates in organic synthesis And it might have also biological importance. This type of derivative are prepared by classical methodology using acid catalyst from furan deridative.[9] With green chemistry aspect we have engaged in the development of environmentally benign reactions. Ideally the use of molecular oxygen as a source for the oxidation and oxidative functionalization of C-H bonds under mild reaction conditions to construct various oxygenated molecules would be the most important approach and considered to be an essential area of research.[10] Molecular oxygen is a desirable source to incorporate in organic molecule as it is environmentally safe and abundantly available.[11] Considering the importance of oxygen incorporation in organic molecules, a number of transition metal catalysts have been developed, but limited reports exist for such activation of molecular oxygen under metal-free conditions.[12] Catalyst free ring opening of substituted furan derivatives with the help of molecular oxygen to form different substituted But-2-ene-1,4-dione at room temperature opens a new strategy in organic synthesis. These 2,3,5-Substituted furan moieties have been prepared with large quantity *via* tandem cycloaddition of ketone with unsaturated carboxylic acid under air (Scheme-1).

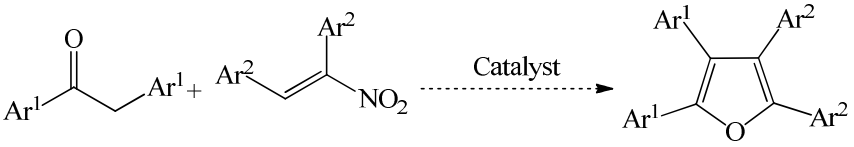


Scheme-1

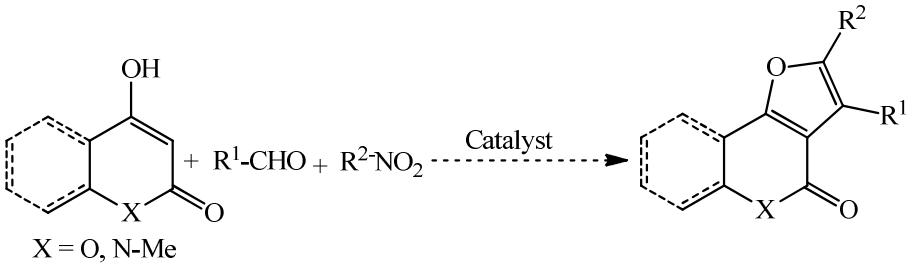
Work Plan:



Scheme 2: Synthesis of Multisubstituted furans from Nitroolefins.



Scheme 3: Synthesis of tetrasubstituted furans.



Scheme 4: Multi-component synthesis of furan derivatives.

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